Manganese in the Environment and Workplace

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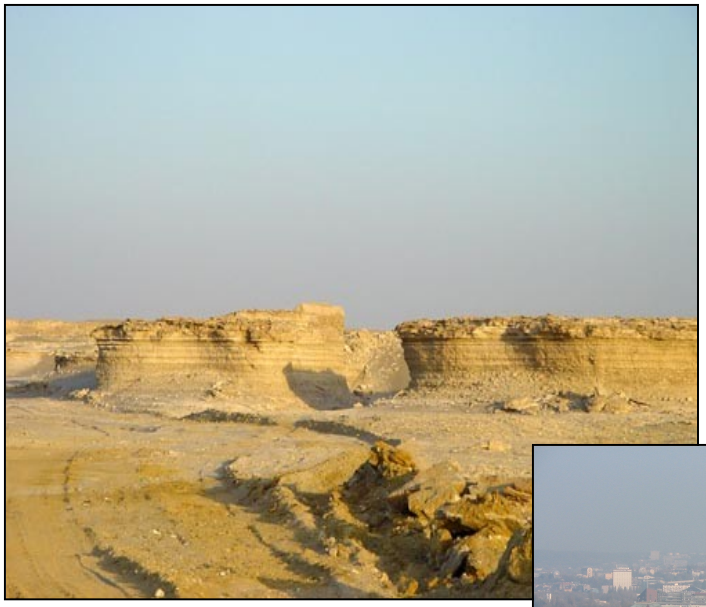
Questions that will be answered in this presentation

- How are we exposed to manganese?
- What are the sources and Mn exposure levels in the environment?
- What are the sources and Mn exposure levels in the workplace?
- What exposure levels of Mn are associated with adverse effects?
- What are the current and proposed regulations for Mn?

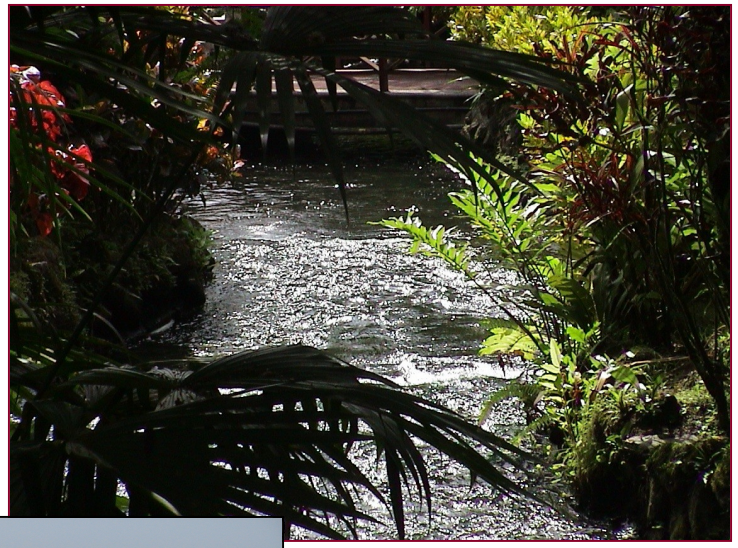
Manganese is an Essential Element

- **Manganese is an essential trace element and is necessary for maintaining good health**
- **Manganese is the 12th most-abundant element in the earth's crust**
- **Manganese is naturally present in soil, water, air, and food**

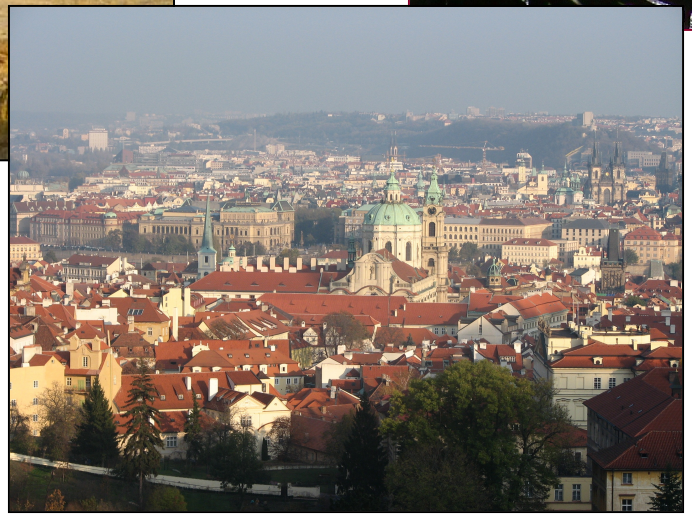
Mn Occurs Naturally in the Environment



Mn natural soil concentration:
40 to 900 mg/kg



Mn natural fresh water concentration:
0.3 to 3,230 µg/L



Mn natural air concentration:
0.01 to 0.07 µg/m^3

Mn is in Food and Drinking Water

99.8% of daily Mn intake is from food and drinking water

ATSDR 2000

A cup of tea contains 1,200 µg Mn

One banana contains 225 µg of Mn

Drinking water typically contains Mn; World Health Organization health-based standard < 500 µg/L

Man-made Sources of Mn in the Environment

Metal alloy production (steel)

Dry-cell batteries

Welding, welding rods

MMT® fuel additive

Maneb (crop fungicide)

Occupational Groups Potentially Exposed to Manganese

- Inorganic compounds:
  - Mn miners
  - Producers of Mn alloys (e.g., steel)
  - Dry alkaline battery manufacturers
  - Aluminum-Mn can producers
  - Smelter and foundry workers (Mn processing and ferro-Mn operations)
  - Welders
- Organic compounds:
  - Agrochemical/pesticide workers (e.g., Maneb, Mancozeb)
  - MMT workers

Department of Defense and Mn

- Welding, metal cutting, and grinding activities
- Considering the use of electroplated aluminum-manganese coatings in place of cadmium coatings for defense systems
- Portable power sources (batteries)

Department of Defense and Mn

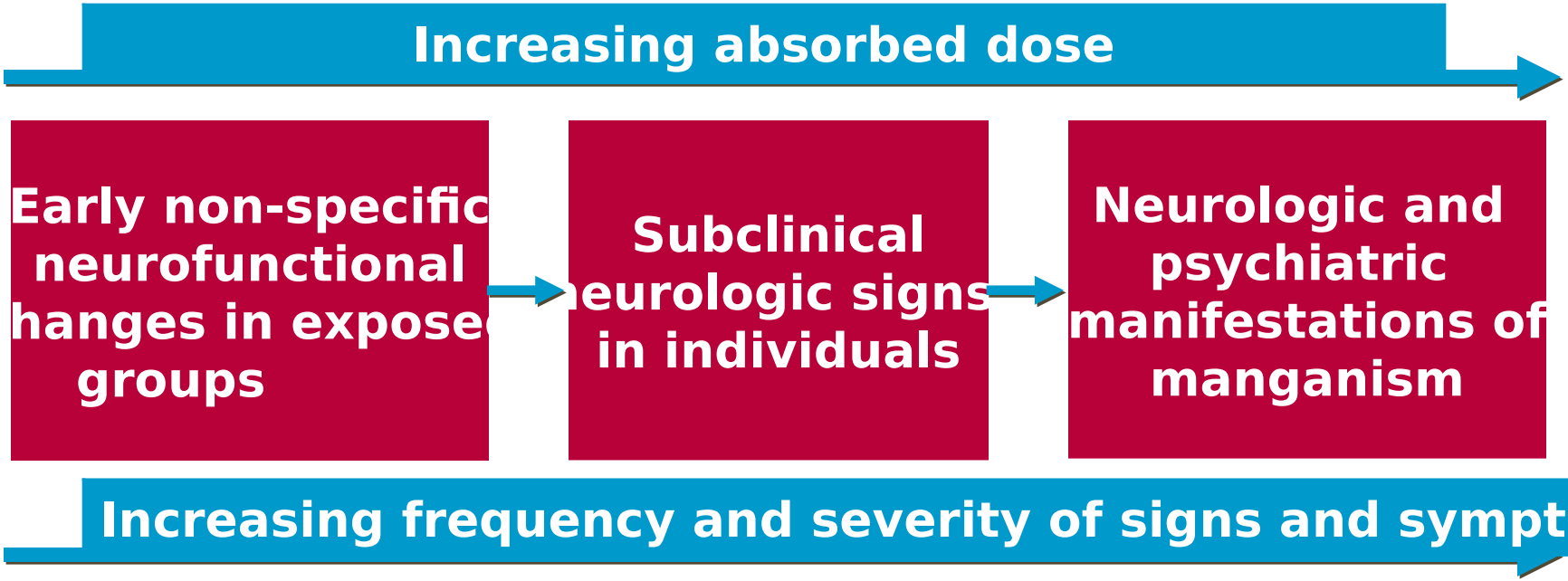
- Manganese Health Research Program (MHRP)
  - This comprehensive, multidisciplinary program is a joint collaboration between the Department of Defense and the manganese industry
  - Conduct human studies and develop animal models
  - Supported by the US Army Medical Research and Material Command (USAMRMC)

MHRP
The Manganese Health Research Program

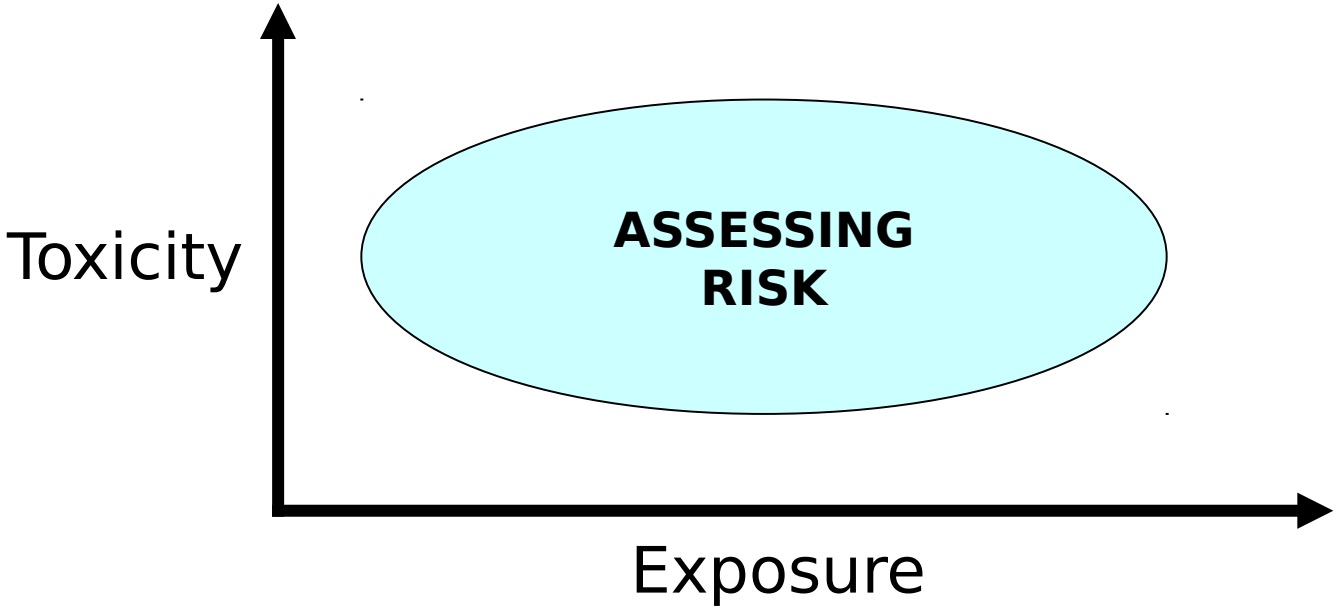
Can we be exposed to too much manganese?

- >99% of manganese intake comes from food and water (average dietary intake ranges from 2 to 10 mg per day for an adult)
- Only a very small amount of Mn is normally taken into the body by inhalation (approximately 0.4 µg/day for an adult).
- Adverse neurological effects have been reported in certain occupations where workers were exposed to high concentrations of manganese-containing dust
  - Typically exposures greater than 1,000 µg/m^3 for prolonged periods of time

Manganese Neurotoxicity


Increasing absorbed dose
Early non-specific neurofunctional hanges in expose groups
Subclinical eurologic signs in individuals
Neurologic and psychiatric manifestations of manganism
Increasing frequency and severity of signs and symptoms

Risk = Exposure x Toxicity

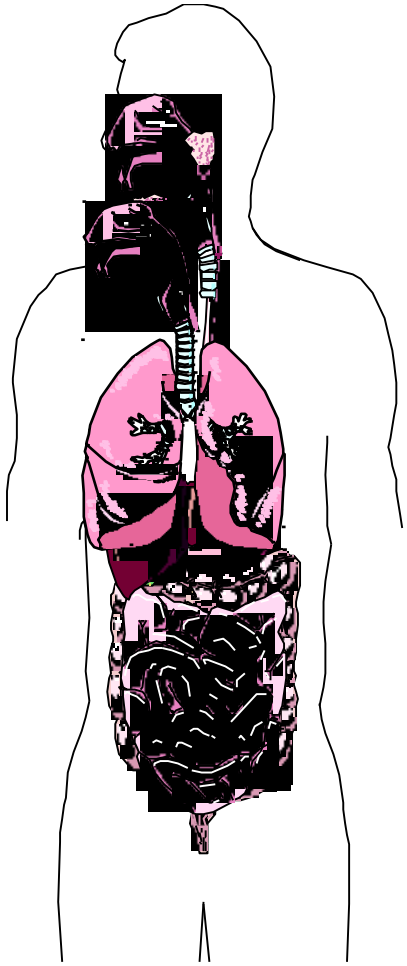


Evaluating Exposure vs. Dose

SOURCES

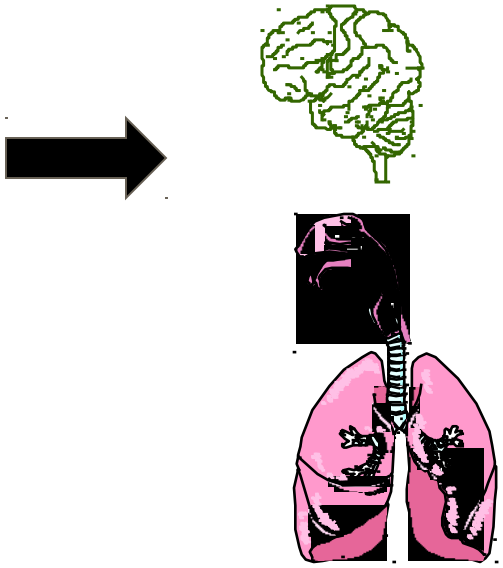
Diet
Environment

EXPOSURE



Mechanisms determining uptake and

DOSE TO TARGET TISSUE



Mechanisms of damage and repair

The important issue is dose to the target tissue, not dose entering the body.

[EPA, ORD 1990]

Critical Risk Assessment Issues – Welders

- What is known regarding Mn dose-response and effects thresholds?
- Are welding exposures sufficiently characterized to permit individual exposure reconstruction?
- Are epidemiology studies of welders consistent with the dose-response information?

Mn Studies in Welders

Study	Mn Level (mg/m^3)	Health Effects	Comment
Chandra et al. (1980)	0.44–2.6	↑ Mn in urine; brisk reflexes; tremors	60 welders; 3 plants; no details about length/freq of sampling and no correlation between exposure and effects
Sjogren et al. (1996)	0.1–0.9 (3 TWAs)	↓↑ Motor function; fatigue	12 welders; no details about TWA sampling
Korcynski (2000)	0.01–4.93 (mean = 0.5)	No CNS effects	42 welders; inside welding helmet
Luse et al. (2000)	0.003–2.6	↓ Motor function and attention tests; blood Mn	46 welders; no details about sampling – “air of work environment”
Sinczuk-Walczak et al. (2001)	0.04–2.67 (mean = 0.4)	Subclinical neuropsych effects	62 welders and fitters; Mn concentrations in “ambient air at workposts”

Data Needs for Exposure Reconstruction

- Simultaneous samples inside vs. outside helmet
- Direct vs. “bystander” exposure
- More TWA data
- Peak exposure data not useful for developing cumulative dose estimates
- Predictive model with field-validation

Example Exposure Levels for Miners, Millers, Smelter, and Battery Workers

Study	Mn Level (mg/m³)	Comment
Hochberg et al. 1996	62.5–250	Mn mine
Rodier 1955	65–926	Mn mine, Morocco
Schuler et al. 1957	0.5–46.0	Mn mine, Chile
Huang et al. 1989 & 1993	Up to 28.8	Ferromanganese smelters
Chia et al. 1993a,b	1.59	Mn milling
Sumitra & Kongsombatsuk 1990	0.02–41.1	Battery factory, Thailand

Mean Mn TWAs in Occupations Measuring Subclinical Effects

Study	Mean Respirable Mn (mg/m^3)	Industry
Roels et al. 1992	0.30 (Effects)	Alkaline Battery
Iregren 1990	0.25 (Effects)	Foundry
Järvisalo et al. 1992	1.37 (Effects)	Welders
Mergler et al. 1994	0.12 (Effects)	Mn Alloy
Gibbs et al. 1999	0.066 (No effects)	Mn Alloy
Deschamps et al. 2001	0.057 (No effects)	Enamels

Conclusions About Occupational Exposure

- Exposure up to 0.2 mg Mn/m^3 unlikely to cause subclinical effects
- Clinical threshold not well-defined; likely to be >1-5 mg/m^3 TWA
- Mn in welding fumes may be less bioavailable
- Pharmacokinetic models will help develop critical dose-response information that will help refine risk assessments

Limitations in Occupational Studies

- Multiple tests; no correction for multiple comparisons
- Self-reported exposure
- Self-reported neurological effects
- Al, Pb, solvents are potential confounders for nervous system effects
- Other potential confounders not controlled for (alcohol consumption, familial history)
- Experimental design concerns

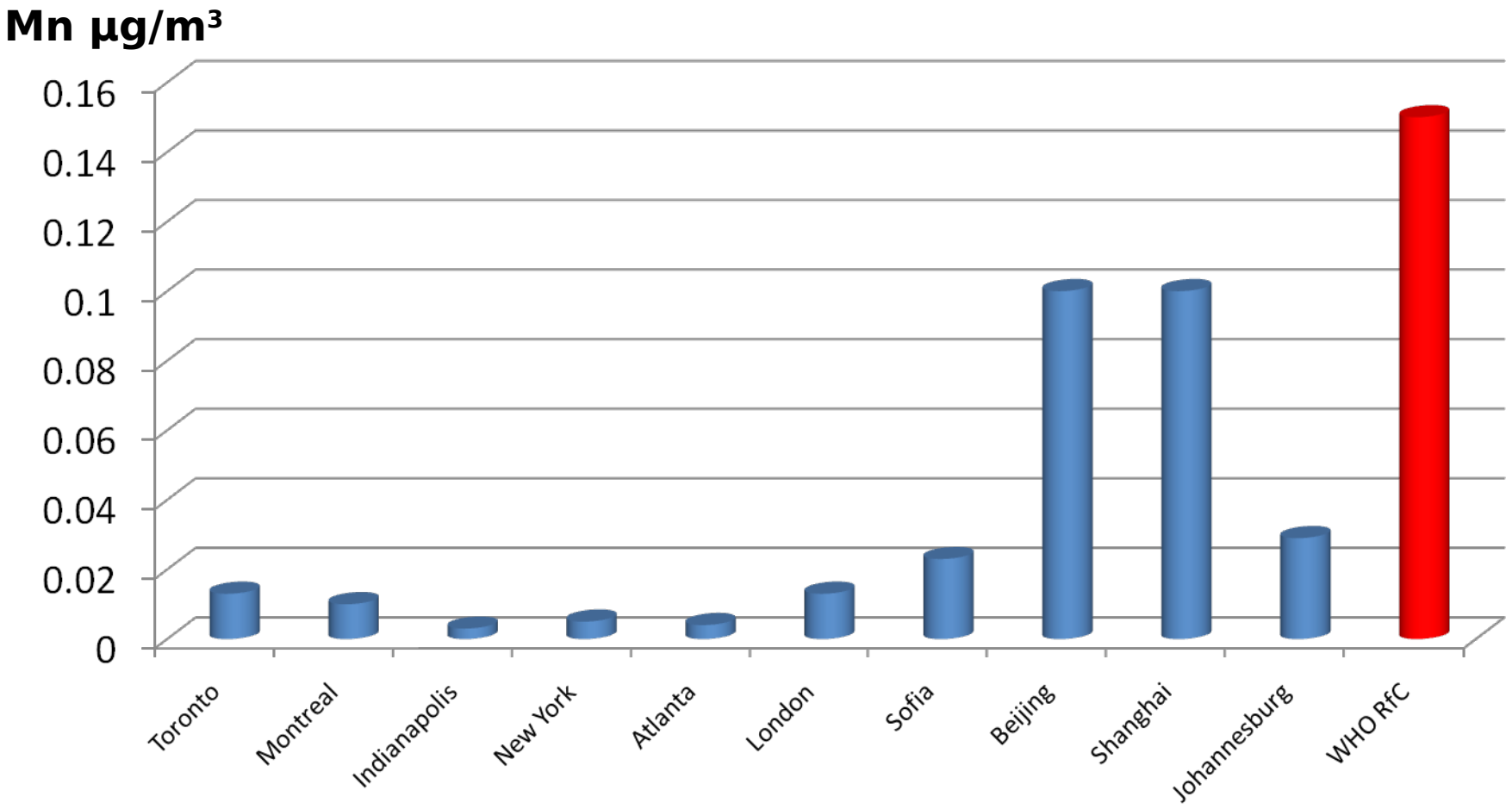
Exposure and Risk

- To estimate risk, the measured exposure level of Mn in the environment or workplace can be compared to the exposure level that is considered to be safe for continuous exposure
- Exposure guidelines are established by regulatory agencies such as OSHA, WHO, USEPA, or the Environmental Health organizations within specific countries or states (e.g., Health Canada, California)
- Environmental regulations for Mn are very protective values with very large safety factors, to protect all members of the population

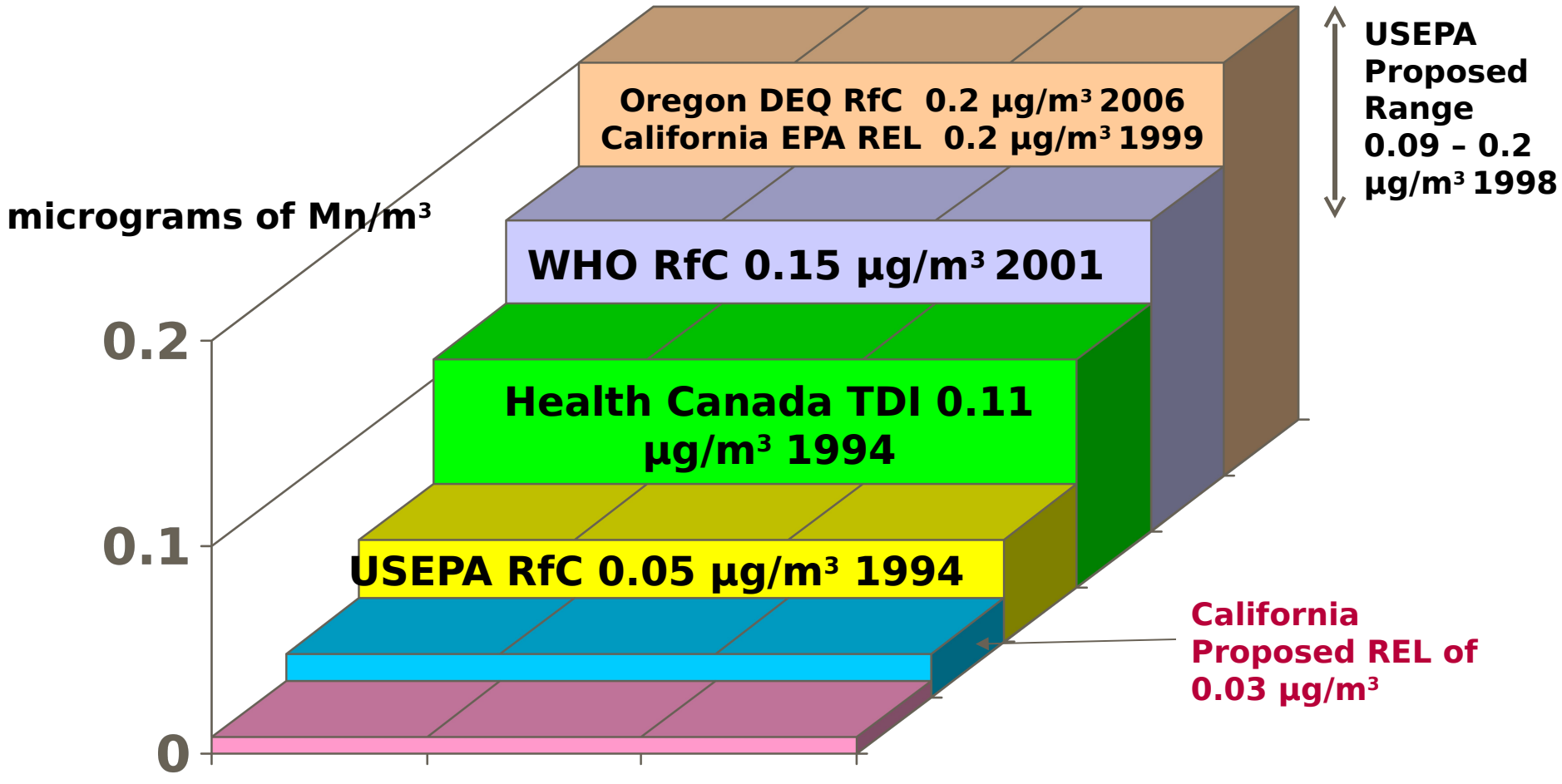
Occupational Limits

- OSHA
  - Mn - PEL TWA
    - 1 mg/m^3
    - 5 mg/m^3 (as ceiling limit)
  - PEL TWA for total welding fumes (total particulate):
    - 5 mg/m^3
- NIOSH
  - TLV REL TWA for Mn compounds:
    - 1 mg/m^3
- ACGIH
  - TLV_{Mn} 0.2 mg/m^3 as TWA

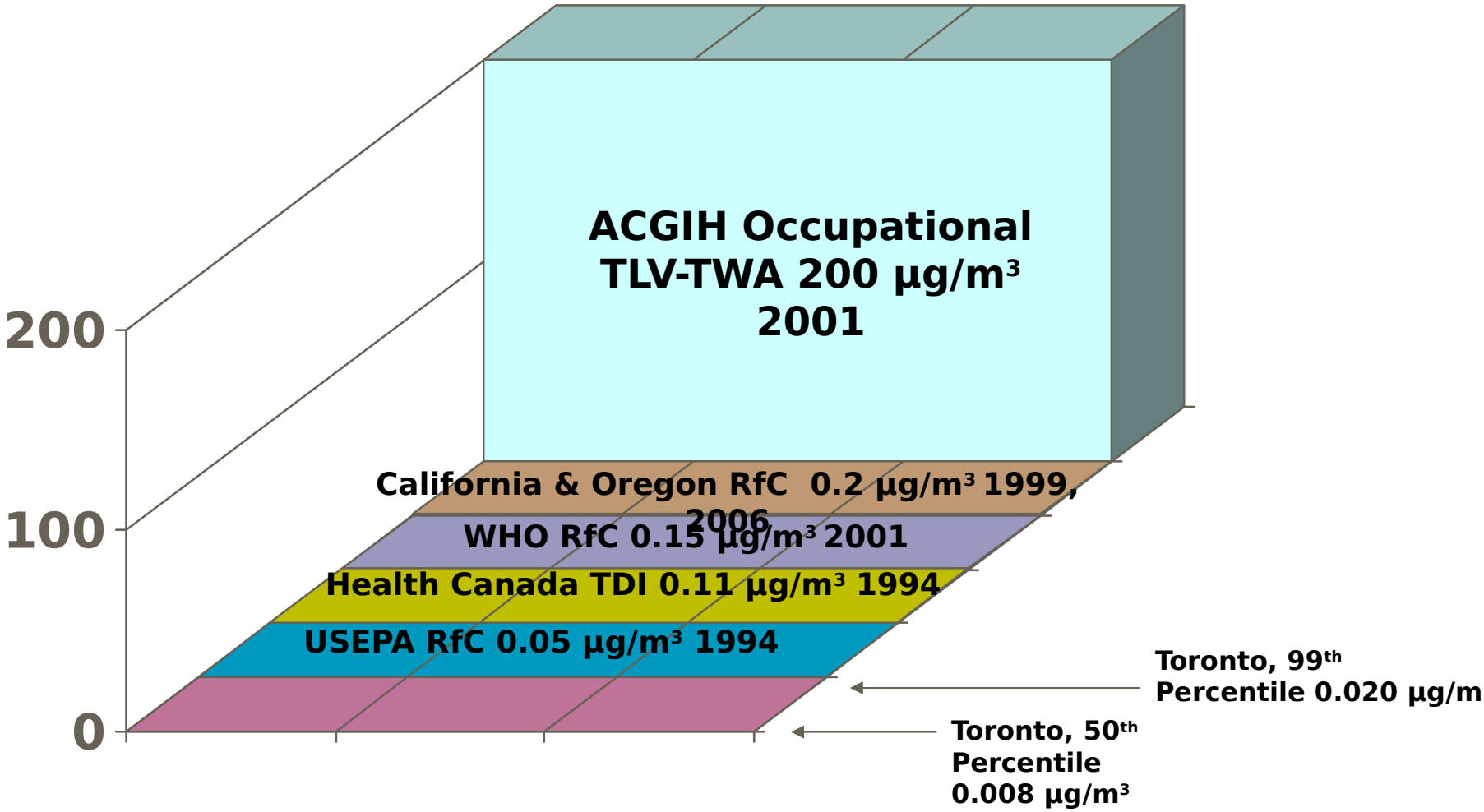
Mean Mn Personal Exposures $PM_{2.5}$ in Major World Cities Compared to WHO Reference Concentration



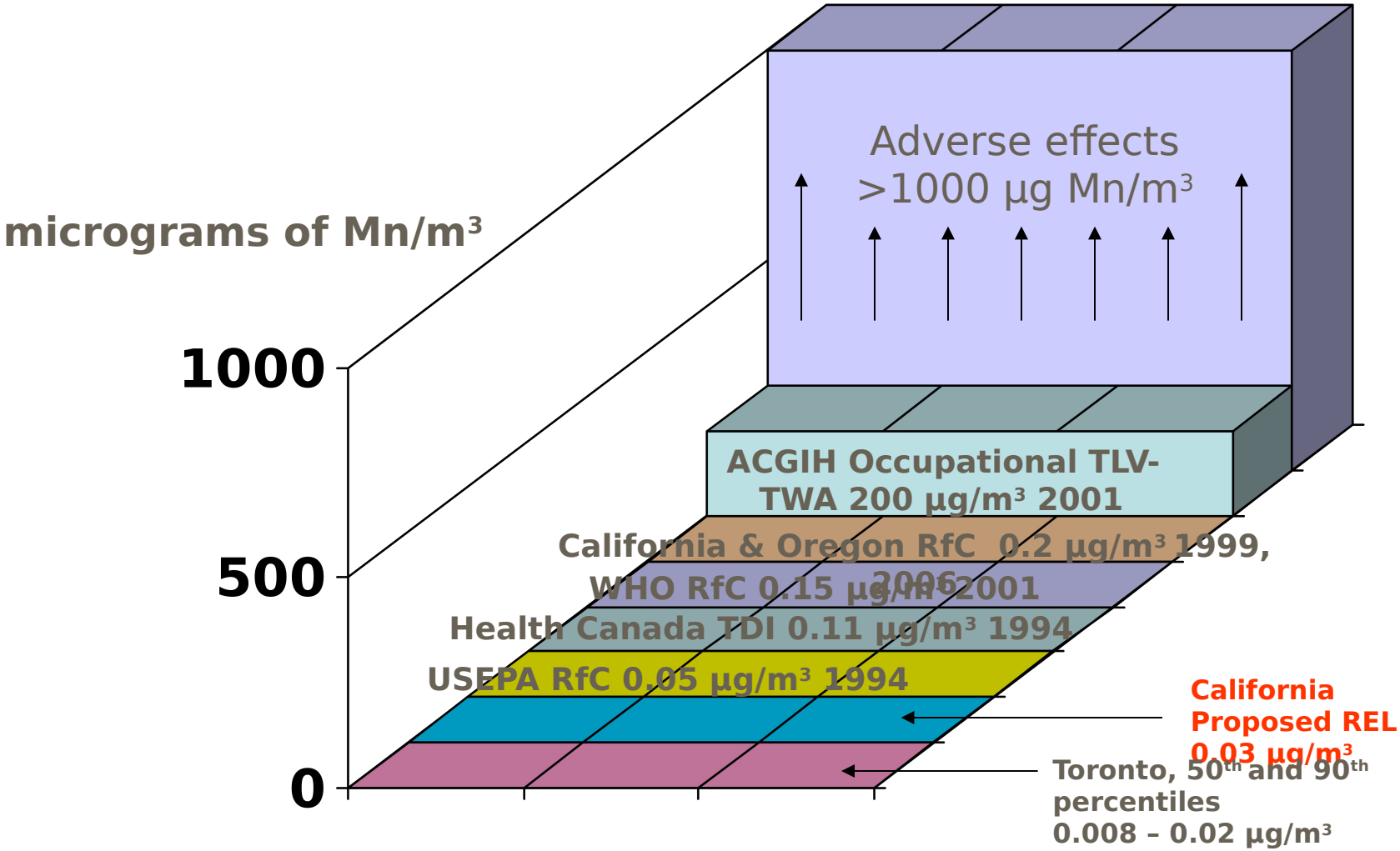
Mn Environmental Guidelines


micrograms of Mn/m³
0.2
0.1
0
Oregon DEQ RfC 0.2 µg/m³ 2006
California EPA REL 0.2 µg/m³ 1999
WHO RfC 0.15 µg/m³ 2001
Health Canada TDI 0.11 µg/m³ 1994
USEPA RfC 0.05 µg/m³ 1994
USEPA Proposed Range 0.09 – 0.2 µg/m³ 1998
California Proposed REL of 0.03 µg/m³

Environmental guidelines are 1,000 to 4,000 times lower than occupational exposure guidelines
Exposure levels are ~25,000 lower



Environmental exposure levels are ~125,000 times lower than exposures reported to be associated with adverse effects in the workplace

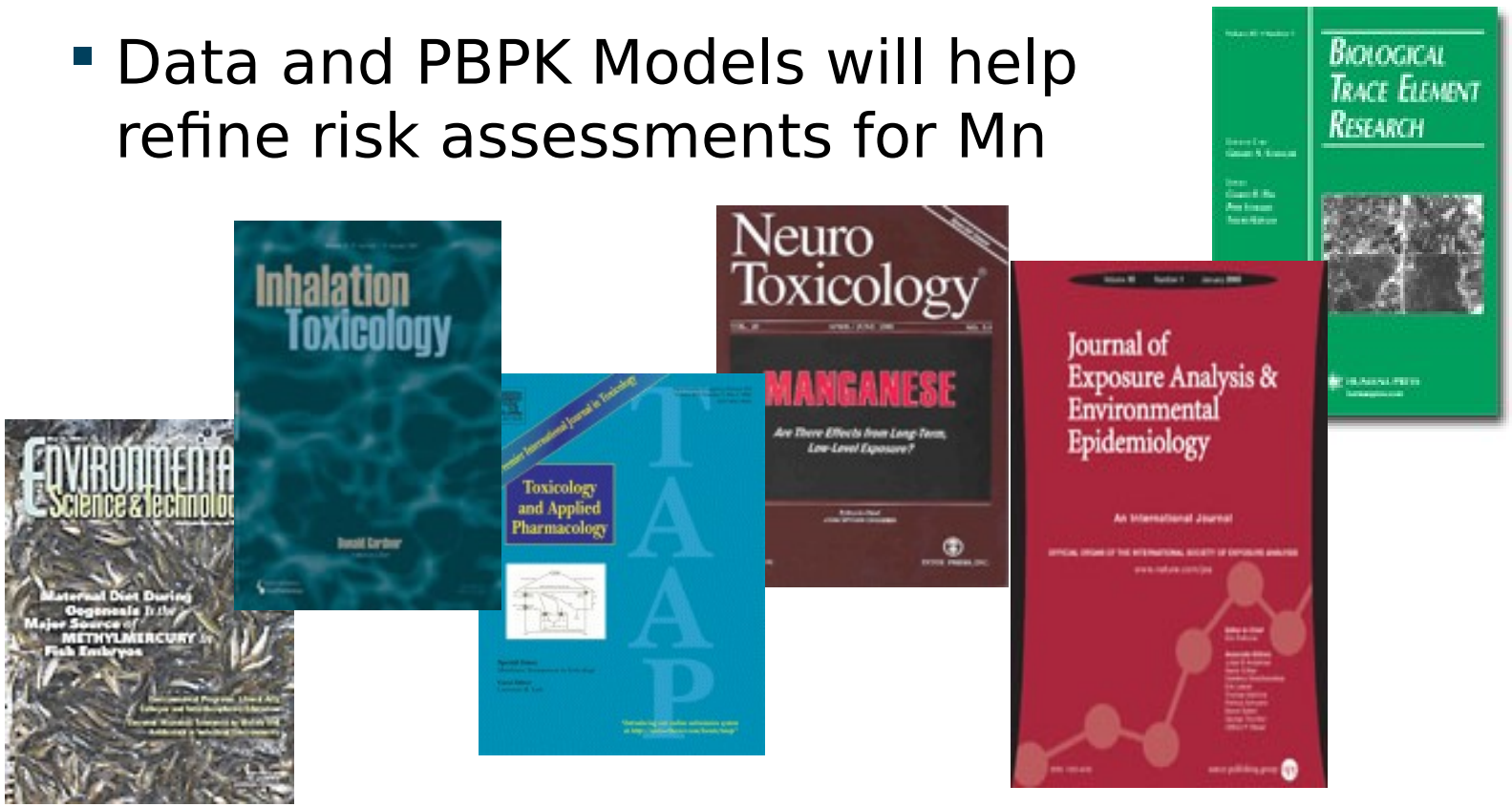


New Tools to Improve Risk Assessment

- Overall Goal: Develop a Physiologically Based Pharmacokinetic (PBPK) model to predict Mn disposition in rats and nonhuman primates following exposure to $MnSO_4$, Mn_3O_4, and $MnHPO_4$
  - Variable exposure concentration and duration
  - Susceptible subpopulations (age, gender, gestation, lactation)
  - Species differences (rat vs. primate)
  - Relative deposition and accumulation in target tissues (form of Mn compound)
- This work is being done at the Hamner Institutes for Health Sciences

Will Health Standards be Revised? If so in what direction?

- Years of published research – since standards were modified
- Data and PBPK Models will help refine risk assessments for Mn


Biological Trace Element Research
Neuro Toxicology
MANGANESE
Are There Effects from Long-Term, Low-Level Exposure?
Inhalation Toxicology
Toxicology and Applied Pharmacology
TAAP
Journal of Exposure Analysis & Environmental Epidemiology
An International Journal
Maternal Diet During Oogenesis Is the Major Source of METHYLMERCURY in Fish Embryos

THANK YOU!

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